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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/516,493	03/01/2000	Maureen J. Charron	96700/613	3363

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EXAMINER	
KAUSHAL, SUMESH	
ART UNIT	PAPER NUMBER
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/516,493	CHARRON ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal	1636	

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 June 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's response filed on 06/03/02 has been acknowledged.

Claims 1-16, 19-21 and 25-29 were canceled.
Claims 44-72 were newly filed.
Claims 44-72 were pending and were examined in this office action.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

▷ *If the claims are amended, added and/or canceled in response to this office action the applicants are required to follow Amendment Practice under 37 CFR § 1.121 (http://www.uspto.gov) and A CLEAN COPY OF **ALL** PENDING CLAIMS IS REQUESTED.*

Claim Objections

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 30-58 has been renumbered 44-72.

Claim Rejections - 35 USC § 112

Claim 48 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification *(new matter)* in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The applicant fails to point out where in the specification there is support for the claim limitation "*comprising 12 transmembrane domains as determined by hydropathy plot analysis*".

Claim Rejections - 35 USC § 101 & 35 USC § 112

Claims 44-72 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility, for the same reasons of record as set forth in the office action mailed on 03/01/02.

Claims 44-72 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention, for the same reasons of record as set forth in the office action mailed on 03/01/02.

Lack of Utility and Enablement rejections are discussed together.

The applicant argues that claims as amended do not require GLUTx activity. The applicant argues that the partial sequences provided would be under stood to be the majority portions of an active GLUTx based upon sequence homology, gene expression and hydropathy plot analysis. The applicant argues that the claims have sufficient utility since the claimed nucleic acid can be used as probes to detect abnormal expression of GLUTx (response, pages 6-8).

However, this is not found persuasive because applicant's argument alone cannot take place of evidence lacking in the record. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). The scope of invention as claimed encompasses a nucleotide sequence that hybridize under stringent hybridization conditions to a nucleotide sequence selected from SEQ ID NO: 6, 9 and 11. The instant invention is not considered to have a specific and/or substantial utility because the specification fails to establish that the polynucleotide sequences as claimed encodes a protein which is a member of glucose transporter/sensor/receptor family as shown by structural and/or functional properties. Since, the instant specification fails to disclose an assay to measure the biological activity of GLUTx polypeptides (as claimed), the only unlimited use for the disclosed polnucloetide sequences would be the determination of what is the biological activity of the encoded by the claimed polynucleotides and further search on how to use the discovered protein activity.

The earlier office action clearly states that it is known in the art that glucose transporter/sensor/receptor (GLUT) have very divergent functions. Glucose transport across biological membranes requires the presence of specific integral membrane proteins in mammals that fall into two classes i) Na+/glucose cotransporters and ii) SGLT1 and SGLT2. These transporters are involved in glucose absorption into the body, glucose uptake by the brain, storage in liver, insulin-dependent uptake in muscles and adipocytes, and glucose sensing by pancreatic cells. Furthermore, the GLUTs form a family of highly related hexose transport proteins that belongs to a larger sugar transport superfamily consisting of more than 133 members distributed in a wide variety of species. These carrier proteins are characterized by the presence of 12 putative transmembrane segments (Ibberson et al, page 4607. The state of art at the time of filing further teaches that studies performed with knockout mice have revealed the existence of glucose transport activity that could not be accounted for by any known GLUTs (Ibberson et al, JBC, 275(7):4607-4612, 2000).

In addition, the amino acid sequences encoding **GLUTX1-consensus sequence** comprises 478 amino acids, whereas the disclosed SEQ ID NO:7 (human) is only 453, SEQ ID NO:10 (mouse) is only 165 and SEQ ID NO:12 (rat) is only 94 amino acid long (see Gene Bank AN: AAB66939 in WO200104145, 2001. *see PTO sequence search report*). At best the instant

specification only disclose pieces of GLUTx-like amino acid sequences isolated from human, mouse and rat. The specification as filed fails to disclose that these partial sequences have any GLUTx-like activity explicitly or implicitly as putatively considered by the instant specification.

Furthermore, known glucose transporter GLUT-isoforms differ in their expression in different tissues, in their kinetic characteristics and in their substrate specificity. For example, GLUT1 mediates glucose transport into erythrocytes and through the blood-brain barrier, and appears to provide a basal supply of glucose for most cells. GLUT2 catalyzes glucose uptake into the liver, and is an essential component of the glucose sensing mechanism of the pancreatic cell. GLUT3 is predominantly expressed in neuronal cells, whereas GLUT4 is exclusively found in muscle and adipose tissue. GLUT5 mediates transport of fructose, but probably not glucose, in intestine and spermatozoa. The diverse tissue distribution and the specific functions of GLUT1-GLUT5 appear to indicate that these genes control glucose uptake in mammalian tissues but the possibility that additional unknown sugar transport facilitators also exist (Doege et al, J. Biol. Chem. 275(21):16275-16280, 2000). The instant specification fails to provide any guidance that a nucleotide sequence that hybridize under stringent hybridization conditions to a nucleotide sequence selected from SEQ ID NO: 6, 9 and 11 have any GLUT1, GLUT2, GLUT3, GLUT4 or GLUT5 like activity.

At best, the Office sequence search using the disclosed amino acid sequences matches with GLUTX3 consensus sequences (AN: AAB66941) SEQ ID NO:7 (40%), SEQ ID NO:10 (31%) and SEQ ID NO:12 (42%), but only with very low sequence similarity. Similarly, SEQ ID NO:7 (23%) and SEQ ID NO:12 (30%) matches with GLUTX2 amino acid sequences (AN: AAB66940, AAB66936 respectively), but only with very low sequence similarity. The courts have clearly stated that: "A specification did not disclose what is well known in the art. See, e.g., Hybritech Inc. V. Monoclonal Antibodies, Inc., 802 F. 2d 1367, 1385, 231 USPQ 81, 94(Fed. Cir. 1986). However, that general off-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific material or of any of the conditions under which a process can be carried out, undue experimentation is required: there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to

the process is within the skill of the art. *It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".* Genentech Inc. V. Novo Nordisk A/s, 42 USPQ2d 1005 (CAFC 1997).

Furthermore, it is noted that patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable (*See Brenner v. Manson , 383 U.S. 519, 536, 148 USPQ 689, 696 (1966), Stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion"*) Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.

Considering the state of art *(supra)* and degree of sequence similarly, the only immediate apparent utility for the instant invention would be its further scientific characterization as a putative glucose transporter/sensor/receptor. In view of the foregoing, one skilled in the art would not readily attribute any particular glucose transporter/sensor/receptor-like activity encoded by the instant nucleic acid in view of the low sequence similarity and the lack of sequence conservation therein. In instant case screening of any and all variants of nucleotide sequences (as claimed) for glucose transporter/sensor/receptor-like activity is not considered routine and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore, the asserted use for the claimed nucleic acid is not considered to support by either a specific and/or substantial utility, since no function can be ascribed to the gene.

Claims 44-47 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the same reasons of record as set forth in the office action mailed on 03/01/02.

The applicant fails to address the Written Description requirement in response to the earlier office action. However, in response to Utility and Enablement issues the applicant states that the partial sequences provided would be under stood to be the majority portions of an active GLUTx based upon sequence homology (response, pages 6-8)

This is not found persuasive because the invention of the claims 44-47 encompasses any and all natural and non-natural variants of SEQ ID NO: 6, 9 and 11obtained from any and all organisms. At best, the specification discloses only one variant each for human mouse and rat within the scope of genus comprising the claimed SEQ ID NO:6, 9 and 11. The specification proposes to discover other members of the genus using sequence similarity under stringent hybridization condatios. However, there is no description of mutational sites that exist in nature, and there is no description how the structure of identified nucleic acid sequences relates to the structure of any strictly neutral alleles. The glucose transporter/sensor/receptor (GLUTs) included members that would expect to have widely divergent functional properties (*Supra)*. The general knowledge in the art glucose transporter/sensor/receptor does not provide any indication as how the structure of one allele is representative of other unknown amino acid sequences having concordant or discordant functions. The commons attributes of all glucose transporter/sensor/receptor are not described, and identifying attributes of individual GLUTx-like protein other than SEQ ID NO:6, 9 and 11 are not described. Furthermore, the amino acid sequences encoding GLUTX1-consensus sequence comprises 478 amino acids, whereas the disclosed SEQ ID NO:7 (human) is only 453, SEQ ID NO:10 (mouse) is only 165 and SEQ ID NO:12 (rat) is only 94 amino acid long (see Gene Bank AN: AAB66939 in WO200104145, 2001. *see PTO sequence search report*). The a specification fails to disclose that the partial sequences encodes any GLUTx-like activity explicitly or implicitly as putatively considered by the instant specification.

In addition, the instant specification fails to disclose a representative number GLUTx variant polypeptides that have glucose transporter/sensor/receptor-like activity. The invention as claimed encompasses nucleic acid sequences that hybridize to the nucleic acid sequence of SEQ ID NO: 6, 9 and 11. The variation as claimed even encompasses the conserved motifs that are germane to any glucose transporter/sensor/receptor-like activity. It is general knowledge in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. The variants as claimed are simply computer generated hypothesis because no biological functions has been established even for SEQ ID NO:7, 10 and 12. The mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues.

The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see In re Shokal 113USPQ283(CCPA1957); Purdue Pharma L. P. vs Faulding Inc. 56 USPQ2nd 1481 (CAFC 2000). In addition possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention Pfaff v. Wells Electronics, Inc 48 USPQ2d 1641, 1646 (1998). According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of only one member of this genus is not representative of the variants of genus and is insufficient to support the claim.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is (703) 305-6838. The examiner can normally be reached on Monday-Friday from 9:00 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor IremYucel can be reached on (703) 305-1998. The fax-phone number for the organization where this application or proceeding is assigned as (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst Zeta Adams, whose telephone number is (703) 305-3291.

S. Kaushal
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